SEQUENCE LISTING

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 CHARLES L. SAWYERS
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 KATHERINE CROSBY

<120> METHODS AND MATERIALS FOR EXAMINING PATHWAYS ASSOCIATED WITH GLIOBLASTOMA PROGRESSION

<130> G&C 30435.148USU1

<150> 60/423,777 <151> 2002-11-05

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Val Val Arg Ile Ser Gly Gly Asn Asp Lys Gln Gly Phe Pro Met Lys 50 60

Gln Gly Val Leu Thr His Gly Arg Val Arg Leu Leu Leu Ser Lys Gly 65 70 75 80

His Ser Cys Tyr Arg Pro Arg Arg Thr Gly Glu Arg Lys Arg Lys Ser

Val Arg Gly Cys Ile Val Asp Ala Asn Leu Ser Val Leu Asn Leu Val 100 105 110 Ile Val Lys Lys Gly Glu Lys Asp Ile Pro Gly Leu Thr Asp Thr Thr

115 120 125 Val Pro Arg Arg Leu Gly Pro Lys Arg Ala Ser Arg Ile Arg Lys Leu

130 135 140
Phe Asn Leu Ser Lys Glu Asp Asp Val Arg Gln Tyr Val Val Arg Lys

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\$165\$ \$170\$ \$175\$ Gln Arg Leu Val Thr Pro Arg Val Leu Gln His Lys Arg Arg Ile

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Tyr Ala Lys Leu Leu Ala Lys Arg Met Lys Glu Ala Lys Glu Lys Arg
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Ser 102		Ile	Arg	Pro	Tyr 1030		Asp	Glu	Ile	Val 1039		Leu	Met	Arg	Glu 1040
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			11e)				1385	5				1390)	
		1395	Ala ; Ile			-	1400)				1405	,	_	
	1410)	Ala			1415	5				1420)	-		
1425		014	niu	mu	1430		V 41	ьсц	Olu	1435		ricc	Dy 3		1440
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Trp Gln Lys Ile Leu Met Val Arg Ser Leu Val Val Ser Pro His Glu
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                                          1645
Asp Met Arg Thr Trp Leu Lys Tyr Ala Ser Leu Cys Gly Lys Ser Gly
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Arg Leu Ala Leu Ala His Lys Thr Leu Val Leu Leu Gly Val Asp
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Pro Ser Arg Gln Leu Asp His Pro Leu Pro Thr Val His Pro Gln Val
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Thr Tyr Ala Tyr Met Lys Asn Met Trp Lys Ser Ala Arg Lys Ile Asp
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Ala Phe Gln His Met Gln His Phe Val Gln Thr Met Gln Gln Gln Ala
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Gln His Ala Ile Ala Thr Glu Asp Gln Gln His Lys Gln Glu Leu His
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Lys Leu Met Ala Arg Cys Phe Leu Lys Leu Gly Glu Trp Gln Leu Asn
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                       1800
                                         1805
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Ile Thr Asn Ala Thr Thr Ala Ala Thr Thr Ala Ala Thr Ala Thr Thr
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Arg Val Leu Thr Leu Trp Phe Asp Tyr Gly His Trp Pro Asp Val Asn
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Glu Ala Leu Val Glu Gly Val Lys Ala Ile Gln Ile Asp Thr Trp Leu
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Gln Val Ile Pro Gln Leu Ile Ala Arg Ile Asp Thr Pro Arg Pro Leu
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                            1945
                                              1950
Val Gly Arg Leu Ile His Gln Leu Leu Thr Asp Ile Gly Arg Tyr His
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                                          1965
Pro Gln Ala Leu Ile Tyr Pro Leu Thr Val Ala Ser Lys Ser Thr Thr
                                       1980
Thr Ala Arg His Asn Ala Ala Asn Lys Ile Leu Lys Asn Met Cys Glu
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1985	1990		1995	2000
His Ser Asn Thr			Met Val Ser G	
Ile Arg Val Ala 2020	Ile Leu Trp H		Trp His Glu G	· -
Glu Ala Ser Arg 2035	Leu Tyr Phe G			
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Leu Lys Glu Thr 2065	Ser Phe Asn G 2070	_	Gly Arg Asp I 2075	eu Met Glu 2080
Ala Gln Glu Trp	2085	2090		2095
	0	- 2105	2	2110
Lys Gln Leu Pro 2115		Ser Leu Glu I 2120	Leu Gln Tyr V 2125	al Ser Pro
Lys Leu Leu Met 2130	2135		2140	
Asp Pro Asn Gln 2145	Pro Ile Ile A 2150		Ser Ile Ala F 2155	ro Ser Leu 2160
Gln Val Ile Thr	Ser Lys Gln A 2165	arg Pro Arg I 2170		eu Met Gly 2175
Ser Asn Gly His 2180		he Leu Leu I 2185		lu Asp Leu 190
Arg Gln Asp Glu 2195	2	200	2205	
Leu Ala Asn Asp 2210	2215		2220	
Tyr Ala Val Ile 2225	2230	2	2235	2240
Pro His Cys Asp	2245	2250		2255
Lys Lys Ile Leu 2260	0	2265	2	270
Pro Asp Tyr Asp 2275	2	280	2285	
His Ala Val Asn 2290	2295		2300	
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Thr Arg Ser Leu	Ala Val Met S 2325	Ser Met Val (2330	Gly Tyr Ile I	eu Gly Leu 2335
Gly Asp Arg His 2340	0	2345	2	350
Ile Leu His Ile 2355		sp Cys Phe (360	Glu Val Ala M 2365	let Thr Arg
Glu Lys Phe Pro 2370	2375	_	2380	
Asn Ala Met Glu 2385	2390	- 2	2395	2400
His Thr Val Met	Glu Val Leu A 2405	arg Glu His I 2410	Lys Asp Ser V	al Met Ala 2415
Val Leu Glu Ala 2420	_	sp Pro Leu I 2425	_	arg Leu Met 430
Asp Thr Asn Thr 2435	2	440	2445	
Tyr Ser Ala Gly 2450	2455		2460	
Glu Pro Ala His 2465	2470	2	2475	2480
Ser Phe Ile Gly	Asp Gly Leu V 2485	al Lys Pro (2490	Glu Ala Leu A	sn Lys Lys 2495

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Thr Ser Leu Thr Val Ser Thr Gln Ser Ser Pro Gly Thr Met Met Gln 390 395 Gln Thr Pro Cys Tyr Ser Phe Ala Pro Pro Asn Thr Ser Leu Asn Ser 405 410 Pro Ser Pro Asn Tyr Gln Lys Tyr Thr Tyr Gly Gln Ser Ser Met Ser 420 425 Pro Leu Pro Gln Met Pro Ile Gln Thr Leu Gln Asp Asn Lys Ser Ser 440 Tyr Gly Gly Met Ser Gln Tyr Asn Cys Ala Pro Gly Leu Leu Lys Glu 455 460 Leu Leu Thr Ser Asp Ser Pro Pro His Asn Asp Ile Met Thr Pro Val 470 475 Asp Pro Gly Val Ala Gln Pro Asn Ser Arg Val Leu Gly Gln Asn Val 485 490 Met Met Gly Pro Asn Ser Val Met Ser Thr Tyr Gly Ser Gln Ala Ser 505 His Asn Lys Met Met Asn Pro Ser Ser His Thr His Pro Gly His Ala 520 Gln Gln Thr Ser Ala Val Asn Gly Arg Pro Leu Pro His Thr Val Ser 535 540 Thr Met Pro His Thr Ser Gly Met Asn Arg Leu Thr Gln Val Lys Thr 550 555 Pro Val Gln Val Pro Leu Pro His Pro Met Gln Met Ser Ala Leu Gly 570 565 Gly Tyr Ser Ser Val Ser Ser Cys Asn Gly Tyr Gly Arg Met Gly Leu 585 Leu His Gln Glu Lys Leu Pro Ser Asp Leu Asp Gly Met Phe Ile Glu 600 Arg Leu Asp Cys Asp Met Glu Ser Ile Ile Arg Asn Asp Leu Met Asp 615 620 Gly Asp Thr Leu Asp Phe Asn Phe Asp Asn Val Leu Pro Asn Gln Ser 630 635 Phe Pro His Ser Val Lys Thr Thr Thr His Ser Trp Val Ser Gly 650

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Lys Ile Thr Asp Phe Gly Leu Cys Lys Glu Gly Ile Lys Asp Gly Ala
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Thr Met Lys Thr Phe Cys Gly Thr Pro Glu Tyr Leu Ala Pro Glu Val
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Leu Glu Asp Asn Asp Tyr Gly Arg Ala Val Asp Trp Trp Gly Leu Gly
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Val Val Met Tyr Glu Met Met Cys Gly Arg Leu Pro Phe Tyr Asn Gln
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Asp His Glu Lys Leu Phe Glu Leu Ile Leu Met Glu Glu Ile Arg Phe
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Pro Arg Thr Leu Gly Pro Glu Ala Lys Ser Leu Leu Ser Gly Leu Leu
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Lys Lys Asp Pro Lys Gln Arg Leu Gly Gly Gly Ser Glu Asp Ala Lys
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Glu Ile Met Gln His Arg Phe Phe Ala Gly Ile Val Trp Gln His Val
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Tyr Glu Lys Lys Leu Ser Pro Pro Phe Lys Pro Gln Val Thr Ser Glu
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Asn Ile Asp Asp Val Val Arq Phe Leu Asp Ser Lys His Lys Asn His
Tyr Lys Ile Tyr Asn Leu Cys Ala Glu Arg His Tyr Asp Thr Ala Lys
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Gln Leu Glu Leu Ile Lys. Pro Phe Cys Glu Asp Leu Asp Gln Trp Leu
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Gly Arg Thr Gly Val Met Ile Cys Ala Tyr Leu Leu His Arg Gly Lys
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Asn Glu Gly Thr Gly Lys Ser Ser Trp Trp Ile Ile Asn Pro Asp Gly
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Gly Lys Ser Gly Lys Ala Pro Arg Arg Arg Ala Val Ser Met Asp Asn
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Ser Gly Arg Leu Ser Pro Ile Met Ala Ser Thr Glu Leu Asp Glu Val
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Gln Asp Asp Asp Ala Pro Leu Ser Pro Met Leu Tyr Ser Ser Ser Ala
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Ser Leu Ser Pro Ser Val Ser Lys Pro Cys Thr Val Glu Leu Pro Arg
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Asn Leu Met Asp Asp Leu Leu Asp Asn Ile Thr Leu Pro Pro Ser Gln
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Pro Ser Pro Thr Gly Gly Leu Met Gln Arg Ser Ser Phe Pro Tyr
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His Ser Asp Val Met Met Thr Gln Ser Asp Pro Leu Met Ser Gln Ala
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Asn Asp Pro Met Met Ser Phe Ala Ala Gln Pro Asn Gln Gly Ser Leu
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Val Asn Gln Asn Leu Leu His His Gln His Gln Thr Gln Gly Ala Leu
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Gly Gly Ser Arg Ala Leu Ser Asn Ser Val Ser Asn Met Gly Leu Ser
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                                       555
Glu Ser Ser Ser Leu Gly Ser Ala Lys His Gln Gln Gln Ser Pro Val
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Ser Gln Ser Met Gln Thr Leu Ser Asp Ser Leu Ser Gly Ser Ser Leu
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Tyr Ser Thr Ser Ala Asn Leu Pro Val Met Gly His Glu Lys Phe Pro
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Ser Asp Leu Asp Leu Asp Met Phe Asn Gly Ser Leu Glu Cys Asp Met
                       615
Glu Ser Ile Ile Arg Ser Glu Leu Met Asp Ala Asp Gly Leu Asp Phe
                   630
                                       635
Asn Phe Asp Ser Leu Ile Ser Thr Gln Asn Val Val Gly Leu Asn Val
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Gly Asn Phe Thr Gly Ala Lys Gln Ala Ser Ser Gln Ser Trp Val Pro
Gly
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                                      475
Phe Gly Thr Ser Gly Gln Lys Thr Lys Ile Ile Ser Asn Arg Gly Glu
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Asn Ser Cys Lys Ala Thr Gly Gln Val Cys His Ala Leu Cys Ser Pro
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Glu Gly Cys Trp Gly Pro Glu Pro Arg Asp Cys Val Ser Cys Arg Asn
       515
                        520
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Val Ser Arg Gly Arg Glu Cys Val Asp Lys Cys Asn Leu Leu Glu Gly
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                                           540
Glu Pro Arg Glu Phe Val Glu Asn Ser Glu Cys Ile Gln Cys His Pro
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Glu Cys Leu Pro Gln Ala Met Asn Ile Thr Cys Thr Gly Arg Gly Pro
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Asp Asn Cys Ile Gln Cys Ala His Tyr Ile Asp Gly Pro His Cys Val
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Lys Thr Cys Pro Ala Gly Val Met Gly Glu Asn Asn Thr Leu Val Trp
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                           600
Lys Tyr Ala Asp Ala Gly His Val Cys His Leu Cys His Pro Asn Cys
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Thr Tyr Gly Cys Thr Gly Pro Gly Leu Glu Gly Cys Pro Thr Asn Gly
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Pro Lys Ile Pro Ser Ile Ala Thr Gly Met Val Gly Ala Leu Leu Leu
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Leu Leu Val Val Ala Leu Gly Ile Gly Leu Phe Met Arg Arg His
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Ile Val Arg Lys Arg Thr Leu Arg Arg Leu Leu Gln Glu Arg Glu Leu
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                                              685
Val Glu Pro Leu Thr Pro Ser Gly Glu Ala Pro Asn Gln Ala Leu Leu
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                                           700
Arg Ile Leu Lys Glu Thr Glu Phe Lys Lys Ile Lys Val Leu Gly Ser
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Gly Ala Phe Gly Thr Val Tyr Lys Gly Leu Trp Ile Pro Glu Gly Glu
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Lys Val Lys Ile Pro Val Ala Ile Lys Glu Leu Arg Glu Ala Thr Ser
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Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Ser
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Val Asp Asn Pro His Val Cys Arg Leu Leu Gly Ile Cys Leu Thr Ser
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                                           780
Thr Val Gln Leu Ile Thr Gln Leu Met Pro Phe Gly Cys Leu Leu Asp
                   790
                                      795
Tyr Val Arg Glu His Lys Asp Asn Ile Gly Ser Gln Tyr Leu Leu Asn
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                                  810
Trp Cys Val Gln Ile Ala Lys Gly Met Asn Tyr Leu Glu Asp Arg Arg
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           820
Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Thr Pro
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                                               845
Gln His Val Lys Ile Thr Asp Phe Gly Leu Ala Lys Leu Leu Gly Ala
                       855
Glu Glu Lys Glu Tyr His Ala Glu Gly Gly Lys Val Pro Ile Lys Trp
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                                       875
Met Ala Leu Glu Ser Ile Leu His Arg Ile Tyr Thr His Gln Ser Asp
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               885
Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ser
                               905
Lys Pro Tyr Asp Gly Ile Pro Ala Ser Glu Ile Ser Ser Ile Leu Glu
                           920
Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr
                       935
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Met Ile Met Val Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys
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Phe Arg Glu Leu Ile Ile Glu Phe Ser Lys Met Ala Arg Asp Pro Gln
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                             970
Arg Tyr Leu Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro
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                          985
                                  990
Thr Asp Ser Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp Met Asp
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                              1005
Asp Val Val Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe
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Ser Ser Pro Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser Ala
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               1030
Thr Ser Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln
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Ser Cys Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg Tyr Ser Ser Asp
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Pro Thr Gly Ala Leu Thr Glu Asp Ser Ile Asp Asp Thr Phe Leu Pro
                      1080 1085
      1075
Val Pro Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser
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                                    1100
Val Gln Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro Ser
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Arg Asp Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn Pro
       1125 1130 1135
Glu Tyr Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe Asp
       1140 1145 1150
Ser Pro Ala His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp
                    1160
     1155
                              1165
Asn Pro Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn
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Ala Pro Gln Ser Ser Glu Phe Ile Gly Ala
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                       40
Gly Glu Gly Ala Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val Arq
                    55
                                    60
Lys Thr Arg Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr
                70
                                75
Tyr Cys Gln Arg Thr Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe Arg
                              90
His Glu Asn Val Ile Gly Ile Arg Asp Ile Leu Arg Ala Ser Thr Leu
                          105
Glu Ala Met Arg Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp
                      120
                                       125
Leu Tyr Lys Leu Leu Lys Ser Gln Gln Leu Ser Asn Asp His Ile Cys
                   135
                                    140
Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala
                150
                               155
Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu Leu Ile Asn Thr
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165

170

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Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala Asp
                                185
Pro Glu His Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg
                           200
Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys
                       215
                                           220
Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser
                   230
                                      235
Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His
               245
                                   250
Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile
                               265
Ile Asn Met Lys Ala Arq Asn Tyr Leu Gln Ser Leu Pro Ser Lys Thr
        275
                            280
Lys Val Ala Trp Ala Lys Leu Phe Pro Lys Ser Asp Ser Lys Ala Leu
                       295
                                            300
Asp Leu Leu Asp Arg Met Leu Thr Phe Asn Pro Asn Lys Arg Ile Thr
                    310
                                        315
Val Glu Glu Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro
                325
                                   330
Thr Asp Glu Pro Val Ala Glu Glu Pro Phe Thr Phe Ala Met Glu Leu
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Asp Asp Leu Pro Lys Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu Thr
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Ala Arg Phe Gln Pro Gly Val Leu Glu Ala Pro
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Cys Lys Ile Glu Ile His Glu Gln Glu Ala Ile Leu His Asn Phe Ser
                       55
Ser Thr Asn Pro Thr Gln Val Asn Gly Ser Val Ile Asp Glu Pro Val
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                                       75
Arg Leu Lys His Gly Asp Val Ile Thr Ile Ile Asp Arg Ser Phe Arg
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                                    90
Tyr Glu Asn Glu Ser Leu Gln Asn Gly Arg Lys Ser Thr Glu Phe Pro
                               105
Arg Lys Ile Arg Glu Gln Glu Pro Ala Arg Arg Val Ser Arg Ser Ser
                            120
Phe Ser Ser Asp Pro Asp Glu Lys Ala Gln Asp Ser Lys Ala Tyr Ser
                       135
                                           140
Lys Ile Thr Glu Gly Lys Val Ser Gly Asn Pro Gln Val His Ile Lys
                   150
                                       155
Asn Val Lys Glu Asp Ser Thr Ala Asp Asp Ser Lys Asp Ser Val Ala
                                    170
Gln Gly Thr Thr Asn Val His Ser Ser Glu His Ala Gly Arg Asn Gly
           180
                               185
Arg Asn Ala Ala Asp Pro Ile Ser Gly Asp Phe Lys Glu Ile Ser Ser
                           200
      195
                                               205
Val Lys Leu Val Ser Arg Tyr Gly Glu Leu Lys Ser Val Pro Thr Thr
                       215
                                           220
Gln Cys Leu Asp Asn Ser Lys Lys Asn Glu Ser Pro Phe Trp Lys Leu
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Tyr Glu Ser Val Lys Lys Glu Leu Asp Val Lys Ser Gln Lys Glu Asn Val Leu Gln Tyr Cys Arg Lys Ser Gly Leu Gln Thr Asp Tyr Ala Thr Glu Lys Glu Ser Ala Asp Gly Leu Gln Gly Glu Thr Gln Leu Leu Val Ser Arg Lys Ser Arg Pro Lys Ser Gly Gly Ser Gly His Ala Val Ala Glu Pro Ala Ser Pro Glu Gln Glu Leu Asp Gln Asn Lys Gly Lys Gly Arg Asp Val Glu Ser Val Gln Thr Pro Ser Lys Ala Val Gly Ala Ser Phe Pro Leu Tyr Glu Pro Ala Lys Met Lys Thr Pro Val'Gln Tyr Ser Gln Gln Gln Asn Ser Pro Gln Lys His Lys Asn Lys Asp Leu Tyr Thr Thr Gly Arg Arg Glu Ser Val Asn Leu Gly Lys Ser Glu Gly Phe Lys Ala Gly Asp Lys Thr Leu Thr Pro Arg Lys Leu Ser Thr Arg Asn Arg Thr Pro Ala Lys Val Glu Asp Ala Ala Asp Ser Ala Thr Lys Pro Glu Asn Leu Ser Ser Lys Thr Arg Gly Ser Ile Pro Thr Asp Val Glu Val Leu Pro Thr Glu Thr Glu Ile His Asn Glu Pro Phe Leu Thr Leu Trp Leu Thr Gln Val Glu Arg Lys Ile Gln Lys Asp Ser Leu Ser Lys Pro Glu Lys Leu Gly Thr Thr Ala Gly Gln Met Cys Ser Gly Leu Pro Gly Leu Ser Ser Val Asp Ile Asn Asn Phe Gly Asp Ser Ile Asn Glu Ser Glu Gly Ile Pro Leu Lys Arg Arg Arg Val Ser Phe Gly Gly His Leu Arg Pro Glu Leu Phe Asp Glu Asn Leu Pro Pro Asn Thr Pro Leu Lys Arg Gly Glu Ala Pro Thr Lys Arg Lys Ser Leu Val Met His Thr Pro Pro Val Leu Lys Lys Ile Ile Lys Glu Gln Pro Gln Pro Ser Gly Lys Gln Glu Ser Gly Ser Glu Ile His Val Glu Val Lys Ala Gln Ser Leu Val Ile Ser Pro Pro Ala Pro Ser Pro Arg Lys Thr Pro Val Ala Ser Asp Gln Arg Arg Ser Cys Lys Thr Ala Pro Ala Ser Ser Ser Lys Ser Gln Thr Glu Val Pro Lys Arg Gly Gly Glu Arg Val Ala Thr Cys Leu Gln Lys Arg Val Ser Ile Ser Arg Ser Gln His Asp Ile Leu Gln Met Ile Cys Ser Lys Arg Arg Ser Gly Ala Ser Glu Ala Asn Leu Ile Val Ala Lys Ser Trp Ala Asp Val Val Lys Leu Gly Ala Lys Gln Thr Gln Thr Lys Val Ile Lys His Gly Pro Gln Arg Ser Met Asn Lys Arg Gln Arg Arg Pro Ala Thr Pro Lys Lys Pro Val Gly Glu Val His Ser Gln Phe Ser Thr Gly His Ala Asn Ser Pro Cys Thr Ile Ile Ile Gly Lys Ala His Thr Glu Lys Val His Val Pro Ala Arg Pro Tyr Arg Val Leu Asn Asn Phe Ile Ser Asn Gln Lys Met Asp Phe Lys Glu Asp Leu

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745
Ser Gly Ile Ala Glu Met Phe Lys Thr Pro Val Lys Glu Gln Pro Gln
               760
Leu Thr Ser Thr Cys His Ile Ala Ile Ser Asn Ser Glu Asn Leu Leu
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                                      780
Gly Lys Gln Phe Gln Gly Thr Asp Ser Gly Glu Glu Pro Leu Leu Pro
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Thr Ser Glu Ser Phe Gly Gly Asn Val Phe Phe Ser Ala Gln Asn Ala
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                              810
Ala Lys Gln Pro Ser Asp Lys Cys Ser Ala Ser Pro Pro Leu Arg Arg
                           825
Gln Cys Ile Arg Glu Asn Gly Asn Val Ala Lys Thr Pro Arg Asn Thr
                        840
Tyr Lys Met Thr Ser Leu Glu Thr Lys Thr Ser Asp Thr Glu Thr Glu
Pro Ser Lys Thr Val Ser Thr Val Asn Arg Ser Gly Arg Ser Thr Glu
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Phe Arg Asn Ile Gln Lys Leu Pro Val Glu Ser Lys Ser Glu Glu Thr
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                                890
Asn Thr Glu Ile Val Glu Cys Ile Leu Lys Arg Gly Gln Lys Ala Thr
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Leu Leu Gln Gln Arg Arg Glu Gly Glu Met Lys Glu Ile Glu Arg Pro
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Phe Glu Thr Tyr Lys Glu Asn Ile Glu Leu Lys Glu Asn Asp Glu Lys
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                                      940
Met Lys Ala Met Lys Arg Ser Arg Thr Trp Gly Gln Lys Cys Ala Pro
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                950
Met Ser Asp Leu Thr Asp Leu Lys Ser Leu Pro Asp Thr Glu Leu Met
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                               970
Lys Asp Thr Ala Arg Gly Gln Asn Leu Leu Gln Thr Gln Asp His Ala
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                           985
Lys Ala Pro Lys Ser Glu Lys Gly Lys Ile Thr Lys Met Pro Cys Gln
                        1000
                                          1005
Ser Leu Gln Pro Glu Pro Ile Asn Thr Pro Thr His Thr Lys Gln Gln
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                                       1020
Leu Lys Ala Ser Leu Gly Lys Val Gly Val Lys Glu Glu Leu Leu Ala
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                        1035
Val Gly Lys Phe Thr Arg Thr Ser Gly Glu Thr Thr His Thr His Arg
                               1050
            1045
Glu Pro Ala Gly Asp Gly Lys Ser Ile Arg Thr Phe Lys Glu Ser Pro
                           1065
         1060
Lys Gln Ile Leu Asp Pro Ala Ala Arg Val Thr Gly Met Lys Lys Trp
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Pro Arg Thr Pro Lys Glu Glu Ala Gln Ser Leu Glu Asp Leu Ala Gly
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                                      1100
Phe Lys Glu Leu Phe Gln Thr Pro Gly Pro Ser Glu Glu Ser Met Thr
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Asp Glu Lys Thr Thr Lys Ile Ala Cys Lys Ser Pro Pro Pro Glu Ser
      1125
                               1130 1135
Val Asp Thr Pro Thr Ser Thr Lys Gln Trp Pro Lys Arg Ser Leu Arg
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         1140
                                              1150
Lys Ala Asp Val Glu Glu Glu Phe Leu Ala Leu Arg Lys Leu Thr Pro
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       1155
Ser Ala Gly Lys Ala Met Leu Thr Pro Lys Pro Ala Gly Gly Asp Glu
                     1175
                                       1180
Lys Asp Ile Lys Ala Phe Met Gly Thr Pro Val Gln Lys Leu Asp Leu
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                                   1195
Ala Gly Thr Leu Pro Gly Ser Lys Arg Gln Leu Gln Thr Pro Lys Glu
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                                1210
Lys Ala Gln Ala Leu Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln
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Thr Pro Gly His Thr Glu Glu Leu Val Ala Ala Gly Lys Thr Thr Lys
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                        1240
                                           1245
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Ile Pro Cys Asp Ser Pro Gln Ser Asp Pro Val Asp Thr Pro Thr Ser
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Thr Lys Gln Arg Pro Lys Arg Ser Ile Arg Lys Ala Asp Val Glu Gly
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Glu Leu Leu Ala Cys Arg Asn Leu Met Pro Ser Ala Gly Lys Ala Met
      1285 1290 1295
His Thr Pro Lys Pro Ser Val Gly Glu Glu Lys Asp Ile Ile Ile Phe
              1305 1310
       1300
Val Gly Thr Pro Val Gln Lys Leu Asp Leu Thr Glu Asn Leu Thr Gly
    1315 1320 1325
Ser Lys Arg Arg Pro Gln Thr Pro Lys Glu Glu Ala Gln Ala Leu Glu
 1330 1335 1340
Asp Leu Thr Gly Phe Lys Glu Leu Phe Gln Thr Pro Gly His Thr Glu
     1350 1355
Glu Ala Val Ala Ala Gly Lys Thr Thr Lys Met Pro Cys Glu Ser Ser
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           1365
Pro Pro Glu Ser Ala Asp Thr Pro Thr Ser Thr Arg Arg Gln Pro Lys
        1380
                       1385
Thr Pro Leu Glu Lys Arg Asp Val Gln Lys Glu Leu Ser Ala Leu Lys
     1395 1400
                                  1405
Lys Leu Thr Gln Thr Ser Gly Glu Thr Thr His Thr Asp Lys Val Pro
 1410 1415 1420
Gly Gly Glu Asp Lys Ser Ile Asn Ala Phe Arg Glu Thr Ala Lys Gln
1425 1430 1435
Lys Leu Asp Pro Ala Ala Ser Val Thr Gly Ser Lys Arg His Pro Lys
          1445
                         1450
Thr Lys Glu Lys Ala Gln Pro Leu Glu Asp Leu Ala Gly Trp Lys Glu
                      1465 1470
Leu Phe Gln Thr Pro Val Cys Thr Asp Lys Pro Thr Thr His Glu Lys
 1475 1480 1485
Thr Thr Lys Ile Ala Cys Arg Ser Gln Pro Asp Pro Val Asp Thr Pro
                               1500
1490 1495
Thr Ser Ser Lys Pro Gln Ser Lys Arg Ser Leu Arg Lys Val Asp Val
    1510 1515
Glu Glu Glu Phe Phe Ala Leu Arg Lys Arg Thr Pro Ser Ala Gly Lys
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Ala Met His Thr Pro Lys Pro Ala Val Ser Gly Glu Lys Asn Ile Tyr
       1540
                      1545 1550
Ala Phe Met Gly Thr Pro Val Gln Lys Leu Asp Leu Thr Glu Asn Leu
   1555 1560 1565
Thr Gly Ser Lys Arg Arg Leu Gln Thr Pro Lys Glu Lys Ala Gln Ala
 1570 1575 1580
Leu Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr Arg Gly His
      1590 1595
Thr Glu Glu Ser Met Thr Asn Asp Lys Thr Ala Lys Val Ala Cys Lys
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Ser Ser Gln Pro Asp Leu Asp Lys Asn Pro Ala Ser Ser Lys Arg Arg
       1620 1625 1630
Leu Lys Thr Ser Leu Gly Lys Val Gly Val Lys Glu Glu Leu Leu Ala
    1635 1640 1645
Val Gly Lys Leu Thr Gln Thr Ser Gly Glu Thr Thr His Thr His Thr
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Glu Pro Thr Gly Asp Gly Lys Ser Met Lys Ala Phe Met Glu Ser Pro
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              1670
Lys Gln Ile Leu Asp Ser Ala Ala Ser Leu Thr Gly Ser Lys Arg Gln
          1685 1690 1695
Leu Arg Thr Pro Lys Gly Lys Ser Glu Val Pro Glu Asp Leu Ala Gly
        1700 1705
                                     1710
Phe Ile Glu Leu Phe Gln Thr Pro Ser His Thr Lys Glu Ser Met Thr
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Asn Glu Lys Thr Thr Lys Val Ser Tyr Arg Ala Ser Gln Pro Asp Leu
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                               1740
Val Asp Thr Pro Thr Ser Ser Lys Pro Gln Pro Lys Arg Ser Leu Arg
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Lys Ala Asp	Thr Glu Glu 1765	Glu Phe Leu	Ala Phe Arg 1770	Lys Gln Thr Pro 1775
Ser Ala Gly	Lys Ala Met 1780	His Thr Pro	_	Val Gly Glu Glu 1790
Lys Asp Ile 179		Leu Gly Thr 1800	Pro Val Gln	Lys Leu Asp Gln 1805
Pro Gly Asn 1810	Leu Pro Gly	Ser Asn Arg 1815	Arg Leu Gln 182	Thr Arg Lys Glu 0
1825	1830)	1835	Glu Leu Phe Gln 1840
	1845		1850	Thr Thr Lys Lys 1855
_	1860	186	5	Thr Pro Thr Asn 1870
187	5	1880		Asp Val Glu Glu 1885
1890		1895	190	
1905	1910	ס	1915	Ile Asn Thr Phe 1920
•	1925		1930	Asn Leu Pro Gly 1935
	1940	194	5	Lys Ala Leu Glu 1950
195	5	1960		Gly His Thr Glu 1965 Cys Lys Ser Pro
1970		1975	198	0
1985	1990	0	1995	Gln Arg Leu Lys 2000 Leu Bro Val Gly
	2005		2010	Leu Pro Val Gly 2015 His Arg Glu Thr
_	2020	202	5	2030 Ser Ala Lys Gln
203		2040	THE LYS GIV	2045
2050		2055	206	
_	Glu Glu Ala 2070		Glu Asp Leu 2075	Ala Gly Phe Lys 2080
2065 Glu Leu Phe				Thr Thr Asp Asp 2095
Lys Thr Thr		Cys Lys Ser	Pro Pro Pro	Glu Ser Met Asp 2110
Thr Pro Thr		Arg Arg Pro	Lys Thr Pro	Leu Gly Lys Arg 2125
Asp Ile Val 2130	Glu Glu Leu	Ser Ala Leu 2135	Lys Gln Leu 214	Thr Gln Thr Thr O
2145	2150	0	2155	Ile Asn Val Phe 2160
_	2165		2170	Ser Val Thr Gly 2175
	2180	218	5	Gln Pro Leu Glu 2190
219	5	2200		Val Cys Thr Asp
2210		2215	222	
Gln Pro Asp 2225	Pro Val Gly 2230		· lle Phe Lys 2235	Pro Gln Ser Lys 2240
				Leu Ala Leu Arg 2255

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                         2265
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Gly Gly Asp Glu Lys Asp Met Lys Ala Phe Met Gly Thr Pro Val Gln
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                             2285
Lys Leu Asp Leu Pro Gly Asn Leu Pro Gly Ser Lys Arg Trp Pro Gln
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                          2300
Thr Pro Lys Glu Lys Ala Gln Ala Leu Glu Asp Leu Ala Gly Phe Lys
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Glu Leu Phe Gln Thr Pro Gly Thr Asp Lys Pro Thr Thr Asp Glu Lys
           2325 2330 2335
Thr Thr Lys Ile Ala Cys Lys Ser Pro Gln Pro Asp Pro Val Asp Thr
        2340 2345 2350
Pro Ala Ser Thr Lys Gln Arg Pro Lys Arg Asn Leu Arg Lys Ala Asp
           2360 - 2365
      2355
Val Glu Glu Phe Leu Ala Leu Arg Lys Arg Thr Pro Ser Ala Gly
                                  2380
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Lys Ala Met Asp Thr Pro Lys Pro Ala Val Ser Asp Glu Lys Asn Ile
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Asn Thr Phe Val Glu Thr Pro Val Gln Lys Leu Asp Leu Leu Gly Asn
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            2405
Leu Pro Gly Ser Lys Arg Gln Pro Gln Thr Pro Lys Glu Lys Ala Glu
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Ala Leu Glu Asp Leu Val Gly Phe Lys Glu Leu Phe Gln Thr Pro Gly
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                                     2445
      2435
His Thr Glu Glu Ser Met Thr Asp Asp Lys Ile Thr Glu Val Ser Cys
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                                  2460
Lys Ser Pro Gln Pro Glu Ser Phe Lys Thr Ser Arg Ser Ser Lys Gln
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               2470
Arg Leu Lys Ile Pro Leu Val Lys Val Asp Met Lys Glu Glu Pro Leu
           2485
                           2490
Ala Val Ser Lys Leu Thr Arg Thr Ser Gly Glu Thr Thr Gln Thr His
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Thr Glu Pro Thr Gly Asp Ser Lys Ser Ile Lys Ala Phe Lys Glu Ser
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Pro Lys Gln Ile Leu Asp Pro Ala Ala Ser Val Thr Gly Ser Arg Arg
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                                  2540
Gln Leu Arg Thr Arg Lys Glu Lys Ala Arg Ala Leu Glu Asp Leu Val
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                              2555
Asp Phe Lys Glu Leu Phe Ser Ala Pro Gly His Thr Glu Glu Ser Met
           2565 2570 2575
Thr Ile Asp Lys Asn Thr Lys Ile Pro Cys Lys Ser Pro Pro Pro Glu
        2580 2585 2590
Leu Thr Asp Thr Ala Thr Ser Thr Lys Arg Cys Pro Lys Thr Arg Pro
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Arg Lys Glu Val Lys Glu Glu Leu Ser Ala Val Glu Arg Leu Thr Gln
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Thr Ser Gly Gln Ser Thr His Thr His Lys Glu Pro Ala Ser Gly Asp
               2630 2635
Glu Gly Ile Lys Val Leu Lys Gln Arg Ala Lys Lys Lys Pro Asn Pro
           2645 2650 2655
Val Glu Glu Glu Pro Ser Arg Arg Pro Arg Ala Pro Lys Glu Lys
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Ala Gln Pro Leu Glu Asp Leu Ala Gly Phe Thr Glu Leu Ser Glu Thr
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Ser Gly His Thr Gln Glu Ser Leu Thr Ala Gly Lys Ala Thr Lys Ile
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                                  2700
Pro Cys Glu Ser Pro Pro Leu Glu Val Val Asp Thr Thr Ala Ser Thr
                               2715
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Lys Arg His Leu Arg Thr Arg Val Gln Lys Val Gln Val Lys Glu Glu
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                            2730
Pro Ser Ala Val Lys Phe Thr Gln Thr Ser Gly Glu Thr Thr Asp Ala
                         2745
Asp Lys Glu Pro Ala Gly Glu Asp Lys Gly Ile Lys Ala Leu Lys Glu
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Ser Ala Lys Gln Thr Pro Ala Pro Ala Ala Ser Val Thr Gl 2770 2775 2780 Arg Arg Pro Arg Ala Pro Arg Glu Ser Ala Gln Ala Ile Gl 2785 2790 Ala Gly Phe Lys Asp Pro Ala Ala Gly His Thr Glu Glu Se 2810 Asp Asp Lys Thr Thr Lys Ile Pro Cys Lys Ser Ser Pro Gl 2825 2825	u Asp Leu 2800 r Met Thr 2815 u Leu Glu 30 a Gln Lys
2785 2790 2795 Ala Gly Phe Lys Asp Pro Ala Ala Gly His Thr Glu Glu Se 2805 2810 Asp Asp Lys Thr Thr Lys Ile Pro Cys Lys Ser Ser Pro Gl	2800 r Met Thr 2815 u Leu Glu 30 a Gln Lys
2805 2810 Asp Asp Lys Thr Thr Lys Ile Pro Cys Lys Ser Ser Pro Gl	2815 u Leu Glu 30 a Gln Lys
	30 a Gln Lys
Asp Thr Ala Thr Ser Ser Lys Arg Arg Pro Arg Thr Arg Al 2835 2840 2845	
Val Glu Val Lys Glu Glu Leu Leu Ala Val Gly Lys Leu Th 2850 2855 2860	
Ser Gly Glu Thr Thr His Thr Asp Lys Glu Pro Val Gly Gl 2865 2870 2875	2880
Gly Thr Lys Ala Phe Lys Gln Pro Ala Lys Arg Asn Val As 2885 2890	2895
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Gln Pro Leu Glu Asp Leu Ala Ser Phe Gln Glu Leu Ser Gl 2915 2920 2925	
Gly His Thr Glu Glu Leu Ala Asn Gly Ala Ala Asp Ser Ph 2930 2935 2940	
Ala Pro Lys Gln Thr Pro Asp Ser Gly Lys Pro Leu Lys Il 2945 . 2950 . 2955 Arg Val Leu Arg Ala Pro Lys Val Glu Pro Val Gly Asp Va	2960
2965 2970 Thr Arg Asp Pro Val Lys Ser Gln Ser Lys Ser Asn Thr Se	2975 ·
	90
2995 3000 3005 Thr Lys Arg Leu Arg Cys Met Pro Ala Pro Glu Glu Ile Va	
3010 3015 3020 Leu Pro Ala Ser Lys Lys Gln Arg Val Ala Pro Arg Ala Ar	
3025 3030 3035	3040
Ser Ser Glu Pro Val Val Ile Met Lys Arg Ser Leu Arg Th	3055
Lys Arg Ile Glu Pro Ala Glu Glu Leu Asn Ser Asn Asp Me 3060 3065 30	70
Asn Lys Glu Glu His Lys Leu Gln Asp Ser Val Pro Glu As 3075 3080 3085	-
Ile Ser Leu Arg Ser Arg Arg Gln Asp Lys Thr Glu Ala Gl 3090 3095 3100 Ile Thr Glu Val Phe Val Leu Ala Glu Arg Ile Glu Ile As	
3105 3110 3115	3120
Glu Lys Lys Pro Met Lys Thr Ser Pro Glu Met Asp Ile Gl 3125 3130	n Asn Pro 3135
Asp Asp Gly Ala Arg Lys Pro Ile Pro Arg Asp Lys Val Th 3140 3145 31	
Lys Arg Cys Leu Arg Ser Ala Arg Gln Asn Glu Ser Ser Gl 3155 3160 3165	
Val Ala Glu Glu Ser Gly Gly Gln Lys Ser Ala Lys Val Le 3170 3175 3180	
Asn Gln Lys Gly Lys Gly Glu Ala Gly Asn Ser Asp Ser Me 3185 3190 3195	3200
Arg Ser Arg Lys Thr Lys Ser Gln Pro Ala Ala Ser Thr Le 3205 3210	u Glu Ser 3215
Lys Ser Val Gln Arg Val Thr Arg Ser Val Lys Arg Cys Al 3220 3225 32	a Glu Asn
Pro Lys Lys Ala Glu Asp Asn Val Cys Val Lys Lys Ile Th 3235 3240 3245	
Ser His Arg Asp Ser Glu Asp Ile 3250 3255	

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Arg Lys Val Ala Thr Glu Phe Glu Ser Phe Ser Phe Asp Ala Thr Phe

His Ala Lys Lys Gln Ile Pro Cys Ile Val Ser Met Leu Thr Lys Glu 250 Leu Tyr Phe Tyr His 275 Leu 275